Oncogenesis: an (almost) indecent proposal

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Abstract

After stating that the understanding of biology can only be achieved through an archaeology point of view, the author presents a theorem by which cancer, as a permanent cell proliferation, is only a biological adaptation function which is the true essence of the evolution of the species. He then tries to demonstrate his theorem, based on the biogenesis complexity and on the fact that all mutagens are oncogenic.

Key words: cancer, mutagenesis, evolution.

We almost always speak of cancer in the present tense, referring to persons in the singular: "the melanoma that killed the patient in bed seven today". Each new case, every day, is a surprise, a disappointment, a desperation in its total opacity. This results in therapeutic doggedness, the courage of the surgeon, the strength of the radiotherapist, and the stubbornness of the chemotherapist.

My discourse has been otherwise, when I have dared to reflect on carcinogenicity. It is not the genesis of this or that cancer that concerns me: it is the intimate nature of oncogenisation that I speak, when I speak. Thus, I shall concern myself with understanding and explaining the process of oncogenicity, as a natural biological event. I shall not propose a theory, but enunciate a theorem. Afterwards they will say whether it is apodictic or aporetic.

In the best Pythagorean tradition, I shall first give the bases, then the enunciation, and finally, the demonstration of my theorem. I have to state up front that demonstration is, absurdly reducing it to what it is, essentially, logical.

Bases

1. The internal logic of Biology is archeological. This means that the manifestations being life forms - all the animals and all the plants that we have out there - of undeniable adaptive genesis, in both time and circumstances, only chronological analysis will enable their meaning to be deciphered (the turtle's shell is no longer absurd, or a tourist and folkloric curiosity, when we discover why it is that the children of the marine turtles are not born in their current habitat, which is in the depths of the seas, but on the sand of the beach; in a drastically shortened time span, through the use of a symbolic program, acquired and miniaturized on the DNA, the turtle hatchlings will pass millions of years of adaptive evolution of the species).

Thus, the meaning of adaptive evolution of biological forms is discovered in time, whereby all biology is archeobiology or else it is nothing; or it is a mere catalog resulting from static, pragmatic descriptions, outside time, and therefore meaningless.

2. The current construction of forms — from the simplest to the most complex, like those of the great metazoans and of man ¾ starts with the zygote, by successive deconstructions that recapitulate the general lines of adaptive evolution.

It was said that ontogenesis recapitulates phylogenesis. But today it is a fascinating reading, which is enriched on a daily basis that we can make of organogenesis. From this perspective, seeing the primitive lung as a derivative of the pharyngeal-esophageal junction is watching the painful progress of many life forms, from the waters and mud of the interior seas to the glory of land life and air breathing.

The pinnacle of this conception will be reached when all the human genome has been deciphered, mapped and cloned, and we can have knowledge of the information that is contained in the major part of our genome that is currently silenced.

I state in advance – it is a prophecy – that this genomic silence contains that the history of the principal evolutive stages that lead an isolated cell to be transformed into man.

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3. Cancer is a biological neoform that is considered absurd because it kills the very beings in which it is constructed. But there are no absurd factors in biology, except when the logic that classifies them thus is a false logic. The archeo-logic that I propose sees the facts in their temporal sequence, in order to decipher their current meaning (logic). Cancer, as a biological fact, is hundreds of millions of years old. It is legitimate to ask: over all this time, what purpose has its capacity to kill served? Was it pure evil, as some pious souls would say? I have therefore laid the foundations to enunciate my theorem.

Theorem

Cancer is a continuous multiplication of cells; cell multiplication with post-mitototic differentiation is the essence of adaptive evolution of the species. Thus, cancer eliminates any genetic patrimony that does not lead to adapted phenotypes (or 'winners'), whether of the cell, the tissue, the organ or the individual, for the benefit of the species. Evolution takes place not in individuals, but in populations.

Cancer is an adaptive biological function and we, mankind, exist today without the exercise of this function, over biological time.

This is the enunciation of the theorem. I shall now demonstrate it.

Demonstration

First argument: Biogenesis of the complexity

In the beginning was the cell, the single-cell, eukaryote organism, with the capacity for permanent multiplication – just like today's cancer cell. Without pressure from the surrounding ecosystem to bring about change, this cell would continue the same way for ever, with genetic information that is only capacitated by the incessant duplication of its DNA, with nothing to stop this incessant activity of multiplication. The principal gene of this isolated cell is the oncogene, and its global program of cell division.

The acquisition of a new capacity, even by a single cell, such as the capacity of an Escherichia coli to synthesize into a new enzyme, requires the emergence of a genetic mechanism that stops the duplication of the DNA so that the cell, no longer dividing, has time to execute and express the neo-information and produce new enzyme; once the production capacity of this enzyme in relation to the effect produced by it has become saturated the brake is attenuated, and the oncogene can recommence cell division.

In the regulation of a cell population, such as the skin, this delicate regulatory mechanism of the effective cells is fully demonstrated, its external regulators being sunlight and mechanical pressure.

The genetically conditioned braking mechanism is called anti-oncogene, and today, the relationship of feedback between anti-oncogene and somatic differentiation, as between oncogene and anti-oncogene, is well-established. The oldest oncogene – i.e. the gene that sparks off the process of normal cell division – has passed through hundreds of millions of stable life in the genome of all cells. And the anti-oncogenes, as they are being discovered, show that they are not as numerous as the types of specific differentiations that generate the complexity of the forms developed over time. The sequence of its appearance is the sequence of adaptive evolution, from the unicellular being to the complex biological forms we see today, including, as all evidence shows, Man.

The cells that do not acquire the new quality in response to adaptive pressure will divide incessantly and die, thereby destroying a non-adapted genome that would have produced a phenotype that was unviable in the new conditions. This selective function of cancer – as a capacity for permanent division – which is evident in unicellular populations persists, in complex form, in multicellular organisms and in even more complex form in multiorgan organisms like Man.

But because the cancer was what enabled the complexity of differentiated cells, tissues and organs that make Man, cancer is not a global disease of Man and his systems of association and integration, but rather, first and foremost, a specific biological event, strictly unicellular in origin, which affects the population of identical cells and only later uses the systems of association and integration to attempt to eliminate the genome of the host which, in the logic of selection by cancer, is a non-adapted genome that produces an unviable phenotype.

A very clear example of this phenomenon is lung cancer in smokers, preceded by an adaptive evolution that generated the pavimentous epithelium to replace the ciliated columnar epithelial cells lining the bronchi, but which is now required to deal with hot smoke instead of air.

Adaptive evolution, as occurs in the human em-

bryo during the development of the zygote, results in the successive elimination of non-adapted cell phenotypes by the mechanism of apoptosis, which is the result of the action on the C-myc oncogene for the privation of growth factors. It is as though the non-adapted cell phenotypes were committing suicide or activating their mechanism of cell division, which is the form of survival but which, for these cell populations, becomes a means of death.

Second argument: Mutagenesis is carcinogenic

All the current mutagens are carcinogenic, just as the mutagens that shaped adaptive evolution were carcinogenic. Therefore, evolution created countless millions of corpses, particularly in the Cambric era. The capacity to cause mutated phenotypes to emerge victorious is based on the mechanism of permanent division for the survival of an altered genome, i.e. oncogenisation. What determines or controls this cancer is the effect of the mutation, in short, the resulting signal of the neo-differentiation. Many cells lose out in this dangerous game; much of the information is destroyed; many complex organisms do not survive, making evolution slow and difficult.

Cancer – i.e. the capacity for permanent division – is a property of all our cell populations, perhaps with the exception of the neurons and striated muscle fiber cells in adults because a high degree of differentiation permanently blocks cell division, clearly preventing any adaptive mutation.

But all the other cells are subject to mutation. The genome is not as stable as molecular biologists thought after the prophetic discovery of Watson and Crick. It is, on the contrary, unstable, sensitive to external actions, and fixes the changes that it suffers, duplicating itself, dividing the cell bodies incessantly, changing the general appearance of the tissue, giving the organ a new function, keeping an organism alive, and enabling the survival of a new population. Mutagenesis is the origin of biodiversity and acts over time, using cell division as its instrument of action.

In our haematopoietic system, particularly in the lymphopoietic system, which is comprised of free, unstructured cells in the tissues or organs, everything occurs as in primordial unicellular beings: the lymphocyte responds to the stimulus that affects the liquid medium in which it lives, with a mutation that leads to the production of a new protein with an original configuration (the antibody, as we call it) and proliferates clonally. Thus, as in Protists, the free cells of the periphery work (these are the plasmocytes), the central cells divide incessantly (these are the staminal lymphocytes, or memory cells). Once the stimulus ends, the clone stops growing: The production of antibodies is a controlled neoplasm.

And the plasma lymphoma? It is an uncontrolled neoplasm, because the protein produced is non-sense in present time, but had meaning in the remote past; is a lymphoma of archeobiological memory (it would take two hours to explain how the protein of the so-called Mediterranean lymphoma emerged in phylogenetic evolution, and how it currently acts in the maintenance of certain lower species of vertebrate). It is said, merely, that the memory of the haematopoietic system is the representation of external factors that put pressure on adaptive evolution and generate the complexity of forms i.e. the biodiversity. As someone once wrote, the immunological system is the image in the mirror, of the universe acting on human beings.

Cancer is an error of mnemic evocation, not controlled by a differentiation that is de-adjusted in time. It is the price to pay for an adaptive evolution that did not delete the traces of our biological history. But its basic mechanism – incessant cell division – is the basic condition of survival in the future, in millions of years to come.

I fear that perhaps I have not managed to convinced anyone, and that my theorem is even an indecent proposal. But I am not alone. The book by James Graham ¾ Cancer Selection. The new theory of evolution ¾ and the two articles that he managed, with great difficulty, to publish in the Journal of Theoretical Biology, expound the same conclusion, though with different bases.

Conclusion

Without the biological mechanism of cancer, there would be no biodiversity. The life of complex beings is only made possible because the force of multiplication is controlled by effective biological mechanisms; but the existence of these mechanisms is proof that the driving force of adaptive evolution is the capacity for permanent division, in short, cancer. ■